10/595,286

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> STR 61825-94-3

WARNING. STEREO DATA NOT INCLUDED IN MODEL (NOT SEARCHABLE)
:END

L2 STRUCTURE CREATED

=> S L2 EXA FUL

FULL SEARCH INITIATED 13:51:36 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 20 TO ITERATE

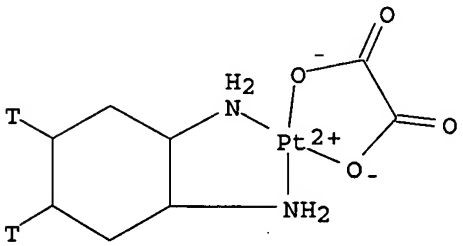
100.0% PROCESSED 20 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

L3 6 SEA EXA FUL L2

=>

=> D SCAN

L3 6 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN Platinum, [rel-(1R,2R,4R,5S)-1,2-cyclohexane-4,5-t2-diamine-κN,κN'][ethanedioato(2-)-κO1,κO2]- (9CI)
MF C8 H12 N2 O4 Pt T2
CI CCS



HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):n

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	58.25	64.98

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FILE COVERS 1907 - 5 Apr 2007 VOL 146 ISS 15
FILE LAST UPDATED: 4 Apr 2007 (20070404/ED)

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=> s l3
L4 1608 L3

=> s l4 and impurities
204170 IMPURITIES
L5 9 L4 AND IMPURITIES

=> d 1-9 bib abs

L5 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:823717 CAPLUS
DN 143:221342
TI An improved process for the preparation platinum(II) 1,2-cyclohexanediamine dicarboxylato complexes for use as anti-tumor agents
IN Maikap, Golak Chandra; Raj, Bhagat; Kumar, Pradipta; Vivekanandan, Kannan; Belwal, Chandrakant
PA Dabur Research Foundation, India
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005075489	A1	20050818	WO 2004-IN35	20040205
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1749015	A1	20070207	EP 2004-708433	20040205
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR				
	IN 2004DN00374	A	20060310	IN 2004-DN374	20040220
PRAI	WO 2004-IN35	W	20040205		

OS CASREACT 143:221342; MARPAT 143:221342
AB Platinum complexes cis-[Q1(NH2)2Pt(O2C)2Q2] [Q1(NH2)2 = cis-, (R,R)-trans-, (S,S)-trans-1,2-cyclohexanediamine; Q2 = cyclo-C(CH2)n, (CH2)n, R3-(un)substituted o-phenylene, n = 0-5, R3 = H, alkoxy, halo, NO2] useful as relatively non-toxic carcinostatic agents (no data), were prepared by reaction of potassium tetrachloroplatinate with Ag2Y (Y = CO3, O; preferably Y = O) in the presence of dicarboxylic acid Q2(CO2H), preferably oxalic acid and cyclohexanediamine or by reaction of cis-[Q1(NH2)2PtX2] (X = carboxylato, sulfonato; preferably X = AcO-,

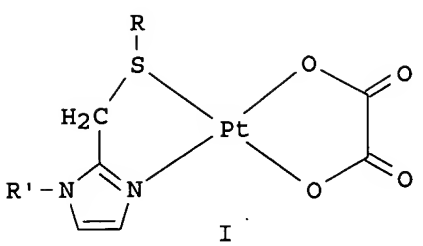
MeSO3-) with alkali metal dicarboxylate, preferably with dipotassium oxalate; the improved process provides high yields of the title complexes and low content of impurities. In an example, cis-[(R,R)-1,2-cyclohexanediamine]diiodoplatinum (1) was prepared by reaction of 0.24 mol of KI and 0.06 mol of K2PtCl4 in 1.5 L of water at 30° for 30 min., followed by addition of 0.06 mol of (R,R)-1,2-cyclohexanediamine; the dichloro-analog cis-[(R,R)-1,2-cyclohexanediamine]dichloroplatinum (2) was prepared in a similar way by reaction of K2PtCl4 and (R,R)-1,2-cyclohexanediamine. The target cis-[(R,R)-1,2-cyclohexanediamine][oxalato(2-)]platinum (Oxaliplatin) was prepared from 1 (0.07 mol) by reaction with 0.07 mol of Ag2O and 0.06 mol of oxalic acid dihydrate; the process does not require addnl. treatment with KI for removal of the remaining silver salts. In other examples, Oxaliplatin was prepared by converting of 2 into cis-bis-acetato or cis-bis-methanesulfonato complexes with subsequent reaction with dipotassium oxalate.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

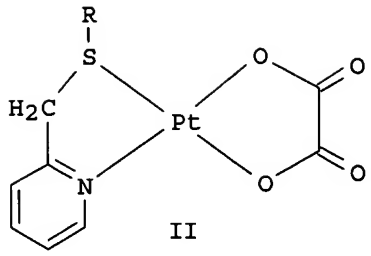
L5 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:493614 CAPLUS
DN 143:37556
TI Preparation of platinum(II) dicarboxylate complexes for use as antitumor agents
IN Du Preez, Jan Gysbert Hermanus
PA Platco Technologies Proprietary Limited, S. Afr.
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005051966	A1	20050609	WO 2004-IB3855	20041124
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2547275	A1	20050609	CA 2004-2547275	20041124
EP 1704156	A1	20060927	EP 2004-798964	20041124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
PRAI US 2003-524727P	P	20031125		
WO 2004-IB3855	W	20041124		

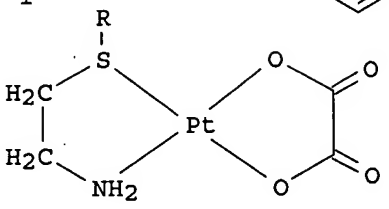
OS CASREACT 143:37556
GI



I



II



III

AB This invention relates to a method for the preparation of platinum(II) complexes, in particular dicarboxylatoplatinum(II) complexes containing a neutral bidentate ligand, such as oxaliplatin. The method includes the step of reacting a bis(dicarboxylato)platinate(II) species with a suitable neutral bidentate ligand to form a neutral dicarboxylatoplatinum(II) complex and, if necessary, recrystg. the product to form a pure dicarboxylatoplatinum(II) complex containing a neutral bidentate ligand. The invention also relates to a method for producing a bis-dicarboxylatoplatinate(II) species, and to new platinum(II) complexes that can be made by the method of the invention. Thus, platinum(II) oxalato complexes (I; R = Me, Bu; R' = Et, Pr, Me and II; R = Me, Et, Pr and III; R = Me, Et, Pr) were prepare and complex I (R = Me, R' = Pr) was tested for antitumor activity.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:347023 CAPLUS
DN 142:384533
TI Improved process for preparation of antitumor agent oxaliplatin with a low content of accompanying impurities of silver, alkali metals and nitrates
IN Zak, Frantisek; Czajka-Poulova, Anna
PA Pliva-Lachema A.S., Czech Rep.
SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005035544	A1	20050421	WO 2004-CZ68	20041014
WO 2005035544	A8	20050909		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CZ 297703	B6	20070307	CZ 2003-2855	20031017

CA 2540374 A1 20050421 CA 2004-2540374 20041014
EP 1680434 A1 20060719 EP 2004-762320 20041014
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR
CN 1867574 A 20061122 CN 2004-80029942 20041014
US 2007073074 A1 20070329 US 2006-595286 20060405
PRAI CZ 2003-2855 A 20031017
WO 2004-CZ68 W 20041014
AB Oxaliplatin, [(1R,2R)-cyclohexanediamine-N,N'][oxalato(2-)]platinum (1), useful as antitumor agent active against colon and rectum malignant tumors (no data) was prepared in pure form containing, by weight, at most 0.01 %, preferably less than 0.001 %, of alkali metals, at most 0.0005 %, preferably less than 0.0002 %, of silver, and at most 0.01 %, preferably less than 0.001 %, of nitrates, by room-temperature reaction of the suspension of dichloro[(1R,2R)-cyclohexanediamine-N,N']platinum with silver nitrate in 1:2 ratio, preferably with 1 mol% excess of AgNO3, followed by treatment with ammonium iodide RR1R2R3NI [R = (un)substituted C1-10 alkyl, (un)substituted C3-10 cycloalkyl; same R1, R2, R3, or R1, R2, R3 = H]; the reaction of the resulting aqueous solution with oxalic acid and recrystn.
of the product 1 from water, washing with polar organic solvent, preferably ethanol. The invented method does not include any reactions with alkali metal salts, which lowers their concentration in the product. In an example, 80.6 g of AgNO3 was added to a suspension of 88.9 g of dichloro[(1R,2R)-cyclohexanediamine-N,N']platinum in 900 mL of water, stirred 70 h at room temperature in the absence of light; after removal of the solids the filtrate was treated with 2,5 g of Et4NI and 0.6 g of activated charcoal. The solution was then reacted with 29.5 g of oxalic acid dihydrate for 4 h, the precipitated oxaliplatin 1 was filtered, dried, recrystd. from water
and washed with 30 mL of water and 400 mL of ethanol, affording 50.2 g of 1 (54% yield). The obtained sample of 1 contained <0.001 wt% of alkali metals, <0.0002 wt% of silver, <0.001 wt% of nitrates and <0.01 wt% of oxalic acid.
RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:138157 CAPLUS
DN 142:204986
TI A thin layer chromatography method to identify oxaliplatin in aqueous solution
AU Hernandez-Trejo, Norma; Hampe, Anja; Mueller, Rainer Helmut
CS Department of Pharmaceutical Technology, Biotechnology & Quality Management, Free University of Berlin, Berlin, Germany
SO Pharmazeutische Industrie (2004), 66(12), 1545-1550
CODEN: PHINAN; ISSN: 0031-711X
PB Editio Cantor Verlag
DT Journal
LA English
AB Within the preparation process of medicines in pharmacies - in addition to having
a recognized anal. certificate - the identity of the drug needs to be confirmed. Ideally this should be done in a non-destructive way that the packaged drug can subsequently still be used for the medicine preparation To achieve this, a new thin layer chromatog. (TLC) method to identify oxaliplatin (CAS 61825-94-3) was developed. This method can be used during the quality assurance of oxaliplatin prepns. for infusion. The method offers the possibility of directly using an aqueous preparation of oxaliplatin instead of an addnl. sample preparation involving the weighing of the drug powder. The main advantage when using aqueous oxaliplatin solns. is the reduction of the occupational risk for the pharmacist when handling hazardous drugs, and the protection of the sterility of the drug powder solution before the administration of the prepns. In the present method a

Silica 60 F254 aluminum sheet is used as a stationary phase and a quaternary mobile phase consisting of methanol-tetrahydrofuran-triethylamine-water (20:2:0.5:1.25 volume/volume). After a development of 8 cm in a presatd. chamber, the chromatog. layer is dried, followed by visual inspection under a UV lamp at 254 nm. Oxaliplatin spots can be detected with a retention factor (rf) of .apprx. 0.7, also after chemical derivatization with specific reagents. The specification of the method is based on the rf comparison of the oxaliplatin spots obtained for a test and a reference solution Addnl., if the intensity of the sample spot lies between the color and the intensity of the reference solution spot, the drug should be identified as oxaliplatin. The selectivity and the intermediate precision of the method were investigated in this study. The first was achieved by comparing oxaliplatin with potential impurities and reference substances, described in the current monograph of the European Pharmacopoeia. After the anal. of a test batch of oxaliplatin by 2 different analysts, no significant differences were observed after statistical comparison of means and variances.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:695773 CAPLUS
DN 137:222017
TI Device for packaging an oxaliplatin solution
IN Ibrahim, Houssam
PA Debiopharm S.A., Switz.
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002069959	A1	20020912	WO 2002-CH133	20020304
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002233104	A1	20020919	AU 2002-233104	20020304
	EP 1368022	A1	20031210	EP 2002-700095	20020304
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	DE 20221679	U1	20061228	DE 2002-20221679	20020304
	US 2004220078	A1	20041104	US 2003-468915	20030825
PRAI	CH 2001-389	A	20010302		
	EP 2002-700095	A	20020304		
	WO 2002-CH133	W	20020304		

AB The invention concerns an assembly consisting of an aqueous oxaliplatin solution and a glass flask containing same , characterized in that the surface/volume ratio of the flask, expressed in mm2/mm3, is less than 0.26. Oxaliplatin solns. were kept in glass flasks with different diams., heights, vols., and surface areas for 10 mo. When the ratio of surface:volume was 0.26 the impurities were 3.66% and when the ratio was 0.17 the impurities were 1.45%.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:682245 CAPLUS
DN 127:302489
TI Process of preparing platinum cyclohexanediamine oxalate complexes of high purity
IN Taniuchi, Jun-ichi; Nakanishi, Chihiro; Ohnishi, Yuko
PA Tanaka Kikinzoku Kogyo K.K., Japan; Dediopharm S.A.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 801070	A2	19971015	EP 1996-830537	19961018
	EP 801070	A3	19980826		
	EP 801070	B1	20030416		
	R: BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT				
	JP 09278785	A	19971028	JP 1996-86954	19960410
	JP 10017587	A	19980120	JP 1996-174788	19960704
	JP 3154399	B2	20010409		
	EP 1308453	A2	20030507	EP 2003-861	19961018
	EP 1308453	A3	20030514		
	R: BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT				
	EP 1308454	A2	20030507	EP 2003-863	19961018
	EP 1308454	A3	20030514		
	EP 1308454	B1	20050601		
	R: BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT				
	PT 801070	T	20030731	PT 1996-830537	19961018
	ES 2194967	T3	20031201	ES 1996-830537	19961018
	PT 1308454	T	20050930	PT 2003-863	19961018
	ES 2243807	T3	20051201	ES 2003-863	19961018
	WO 9801454	A1	19980115	WO 1997-JP2332	19970704
	W: US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 881226	A1	19981202	EP 1997-929532	19970704
	EP 881226	B1	20031126		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	AT 255118	T	20031215	AT 1997-929532	19970704
	PT 881226	T	20040331	PT 1997-929532	19970704
	ES 2210543	T3	20040701	ES 1997-929532	19970704
	US 5959133	A	19990928	US 1998-29682	19980303
PRAI	JP 1996-86954	A	19960410		
	JP 1996-174788	A	19960704		
	EP 1996-830537	A3	19961018		
	WO 1997-JP2332	W	19970704		

OS MARPAT 127:302489
GI For diagram(s), see printed CA Issue.
AB Disclosed are processes for the preparation of platinum cyclohexanediamine oxalate complexes I (R = oxalate, oxalate derivative) with elevated yield and preventing contamination with impurities. Reaction of cis-[diaqua(trans-l-1,2-cyclohexanediamine)platinum(II)] with oxalic acid or oxalate derivative where the pH is adjusted to 3.0-6.0 with an alkali solution, e.g., KOH, affords I (R = oxalate, oxalate derivative). Reaction of a cis-platinum(II) 1,2-cyclohexanediamine dihalo complex (diamine ligand is cis, trans-l or trans-d, halo is Cl or Br) with 2.01-2.1 molar equiv silver ion solution, removing the silver halide produced, adding NaI or KI and active carbon, filtering out impurities, followed by addition of an organic dibasic acid to the filtrate gives oxalate complexes I. The preparation of complexes I starting from potassium or sodium tetrachloroplatinate and the cyclohexanediamine are performed under ≤ 5% O2, or under N2, in vacuo or in an inert gas atmospheric in

deoxygenated water. Thus, for elevating a yield of I and preventing the contamination of impurities, the pH of a solution and an amount of a Ag ion are adjusted, and a reaction environment is so controlled that oxidation is difficult to occur.

L5 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:654969 CAPLUS
DN 127:351345
TI HPLC for determination of impurities in anticancer platinum compounds
IN Onishi, Hiroko
PA Tanaka Kikinzoku Kogyo K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 09257781	A	19971003	JP 1996-67558	19960325
	JP 3118184	B2	20001218		
PRAI	JP 1996-67558		19960325		

AB Impurities in platinum (II) complexes of 1,2-cyclohexanediamine isomers, especially cis-oxalato[trans-(-)-1,2-cyclohexanediamine]platinum (I), are quant. determined by HPLC using ODS column and a mobile phase such as water, acetonitrile, and buffers. The impurities are 1,2-cyclohexanediamine platinum (IV) complexes, such as (trans-R,R-cyclohexane-1,2-diamine)dihydroxo(malonato)platinum. Impurities (i.e. dihydroxy compds.) in I were determined to be 0.12 % by HPLC using Hypersil ODS column (25 cm in length) and water as a mobile phase (flow rate 1 mL/min).

L5 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1995:259901 CAPLUS
DN 122:45003
TI Platinum compound and process of preparing same.
IN Okamoto, Koji; Hoshi, Yuko; Nakanishi, Chihiro
PA Tanaka Kikinzoku Kogyo K.K., Japan
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 617043	A1	19940928	EP 1993-830118	19930325
	EP 617043	B1	20011031		
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
	JP 05194332	A	19930803	JP 1992-23219	19920113
	JP 07076230	B	19950816		
	ES 2166760	T3	20020501	ES 1993-830118	19930325
PRAI	JP 1992-23219		19920113		
	EP 1993-830118	A	19930325		

AB Disclosed herein are a Pt compound employed as raw material of medicines having carcinostatic effects, and a process of preparing the Pt compound The Pt compds. PtLL' (L = 1,2-cyclohexanediamine isomer, L' = OC(O)CH2O, OC(O)C(O)O or OC(O)RC(O)O (R = CH2, CHMe, cyclo-Bu,, C6H3CO2H)) can be prepared substantially free from impurities through a reaction between the corresponding dihalogen compound and an organic dibasic acid employing differences of solubilities. As an example, PtLL' (L = trans-1,2-cyclohexanediamine, L = OC(O)C(O)O) is prepared No antitumor data are reported.

L5 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1988:603718 CAPLUS
DN 109:203718
TI Synthesis and characterization of diastereomeric (substituted iminodiacetato)(1,2-diaminocyclohexane)platinum(II) complexes
AU Hoeschele, James D.; Farrell, N.; Turner, W. R.; Rithner, Christopher D.
CS Parke-Davis Pharm. Res. Div., Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SO Inorganic Chemistry (1988), 27(23), 4106-13
CODEN: INOCAJ; ISSN: 0020-1669
DT Journal
LA English
AB [Pt(DACH)L] [DACH = (R,S)- and (R,R)-1,2-diaminocyclohexane; H2L = RN(CH2CO2H)2, R = Me, CH2CH2OH, CH2Ph] were prepared, purified, and characterized by spectroscopic techniques (1H, 13C, and 195Pt NMR; fast-atom bombardment mass spectra; IR) and by the measurement of selected phys. properties (pH, pKa, conductivity, and mol. wts.). The data are consistent with the formation of 2 diastereomeric complexes in unequal proportions in which L2- appears to be bonded as a pseudofacial tridentate chelate. One arm of the ligand forms a stable 5-membered-ring O,N-chelate while the other arm appears to be involved in ion-pair formation (zwitterion-like) involving the carboxylate anion and the formally pos. Pt(II) central metal atom. An antitumor-active impurity was present in predictably inactive bulk complexes of the type PtN3O. The need to characterize unequivocally and certify the purity of prospective antitumor complexes is emphasized.

=> s l3/prep
1608 L3
4383783 PREP/RL
L6 41 L3/PREP
(L3 (L) PREP/RL)

=> d 1-41 bib abs

L6 ANSWER 1 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1317872 CAPLUS
DN 146:62926
TI Method for refining oxaliplatin
IN Zong, Zaiwei; Chen, Xiangfeng; Wei, Jia
PA Jiangshu Aodesai Pharmaceutical Co., Ltd., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 8pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1876665	A	20061213	CN 2006-10088307	20060710
PRAI CN 2006-10088307		20060710		

AB The title method comprises: (1) dissolving crude oxaliplatin in 40-100°C water at an oxaliplatin/water weight ratio of 5-100, (2) adding C1-3 alkyl alc. 1-5 times the volume of the above oxaliplatin/water solution, (3) cooling for crystallization, (4) filtering, and (5) drying to obtain refined oxalipatin. The method has the advantages of very low oxalic acid content and high refinement yield rate.

L6 ANSWER 2 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1122501 CAPLUS
DN 145:460500
TI Process for production of polymer-type therapeutic agent for treatment of cancer
IN Maeda, Hiroshi; Greish, Khaled

PA Japan
SO PCT Int. Appl., 23pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006112362	A1	20061026	WO 2006-JP307853	20060413

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI JP 2005-120159 A 20050418

AB It is intended to provide a process for polymerizing a low-mol. anti-tumor agent so that the anti-tumor agent can be accumulated in tumor tissues selectively, the process enabling to increase the mol. weight and improve the tumor-selectivity of the anti-tumor agent and to give a product with high purity in simple steps. Disclosed is a process for producing a polymer-type anti-tumor agent, comprising reacting an anhydrous styrene-maleic acid copolymer with a low-mol. therapeutic agent for cancer in the absence of a condensing agent under alkaline conditions, solubilizing the resulting product, adjusting the product to pH 6 to 8, and collecting a polymeric micelle complex having the active agent contained therein by a procedure for separating a polymeric component. Thus, pirarubicin hydrochloride and styrene-maleic acid copolymer were mixed in disodium carbonate at 20-45° for 10 h, and then the pH of the mixture was decreased to 3-5 with a HCl solution After further mixing for 30 min, the pH of the mixture was adjusted to 8-10 with NaHCO3, and the mixture was ultrafiltrated and washed to obtain micelle composite.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1094815 CAPLUS
DN 145:426014
TI A process for the preparation of oxaliplatin formulation
IN Kysilka, Vladimir; Kalisz, Tomas; Kacer, Petr
PA Vuab Pharma A.S., Czech Rep.
SO PCT Int. Appl., 31pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006108428	A1	20061019	WO 2005-EP3746	20050409

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF,

CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI WO 2005-EP3746 20050409

AB The present invention relates to an improved process for the preparation of oxaliplatin, the obtained oxaliplatin preparation and its use in cancer therapy. A mixture of fine powdered 97% (SP-4-2)dichloro-[(1R,2R)-1,2-cyclohexane-kN, kN°]platinum (II) complex, AgNO3 and water was intensively agitated. A 0.1N solution of NaOH was added to the filtrate to adjust the pH to 12, and active carbon at 0.3 g was added to the mixture and stirred for 1 h, the solid fraction was removed by filtration and a cake was properly sucked. The yellow crude alkaline filtrate was poured on a column with wet DOWEX 50W-X8, and the eluent including necessary amount of washing water was concentrated Silica gel was added to the eluent and the filtrate was treated with oxalic acid dihydrate to give oxaliplatin.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1015265 CAPLUS
DN 145:448129
TI Preparation of oxaliplatin as antitumor agent
IN He, Jian; Liu, Weiping; Li, Yongnian; Hou, Shuqian; Pu, Shaoping; Liu, Zhudong
PA Kunming Guiyan Pharmaceutical Co., Ltd., Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 5pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1837223	A	20060927	CN 2006-10010829	20060418
PRAI CN 2006-10010829		20060418		

OS CASREACT 145:448129
AB The title method comprises carrying out reaction between M2PtCl4 (M = K, Na, or Li) and DACH (DACH = trans-1,2-diaminocyclohexane) to obtain dichloro·trans-1,2-diaminocyclohexane Pt (II) complex, carrying out reaction between dichloro·trans-1R,2R-diaminocyclohexane Pt (II) complex and oxalate to obtain oxaliplatin.

L6 ANSWER 5 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:212708 CAPLUS
DN 144:265955
TI Improved process for preparation of platinum(II) oxalate complexes containing neutral bidentate ligand by silver-free anion substitution in organic solvents
IN Du Preez, Jan Gysbert Hermanus
PA Platco Technologies (Proprietary) Limited, S. Afr.
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006024897	A1	20060309	WO 2005-IB570	20050307

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,

IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2004-606119P P 20040901
US 2004-606124P P 20040901

OS CASREACT 144:265955

AB Platinum complexes containing neutral bidentate N, S or Se ligand, preferably platinum oxalates with optically active 1,2-cyclohexanediamine were prepared by silver-free process starting from the corresponding dichloro-compds. by reaction with metal or tetraalkylammonium oxalates, preferably with cesium or tetrabutylammonium oxalates in a solvent wherein more than 1 g/L of the oxalate salt is soluble Preferably, the reaction is performed in organic solvent, typically DMF or DMF-water mixts. at 40-100°, preferably at 60-90° in molar ratio greater than 1:1, preferably the ratio of Pt:C2O4 being between 1:1 and 1.5. Preparation of new platinum complexes containing N,S-bidentate ligands, alkyl pyridinylmethyl sulfide and alkyl 2-imidazolylmethyl sulfide using the same procedure, and their use as anticancer agents is also claimed. In an example, reaction of 10.57 mmol of [Pt[(S,S)-1,2-diaminocyclohexane]Cl2] with 3 equiv of (Bu4N)C2O4 (31.71 mmol) in 520 mL of DMF with addition of 50 mL of water for 4 h at 65°, followed by addition of another 10.57 mmol of [Pt[(S,S)-1,2-diaminocyclohexane]Cl2] in 560 mL of DMF and 58 mL of water at 65° for another 4 h gave 35% of oxaliplatin of 99.94% optical purity and of ≥99.5% chemical purity. In another example, prepared dichloro(1-methyl-2-methylthiomethylimidazole)platinum was tested for anticancer activity, showing 98.2%, 99.3% and 66.1% of inhibition of colon, cervical and breast cancer cells at 100 μM concentration in the presence of 10 mM of glutathione, performing superior to cisplatin.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:170759 CAPLUS
DN 144:204604
TI Cis-diiodo(trans-l-1,2-cyclohexanediamine)platinum(II) complex and processes for preparing high purity oxaliplatin
IN Menez, Guillermo Huerta; Fimognari, Domenico
PA Mex.
SO U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DT Patent
LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006041012	A1	20060223	US 2005-178290	20050712
CA 2573747	A1	20060302	CA 2005-2573747	20050712
WO 2006023154	A1	20060302	WO 2005-US24493	20050712

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP 1658300	A1	20060524	EP 2005-770734	20050712

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,

BA, HR, IS, YU
JP 2007505165 T 20070308 JP 2006-534483 20050712
PRAI US 2004-586729P P 20040712
US 2004-591209P P 20040727
WO 2005-US24493 W 20050712
AB The present invention is related to pure cis-diiodo(trans-l-1,2-cyclohexanediamine)platinum(II) complex, and a process of its preparation The diiodo complex of high purity is prepared by reaction of a mixture of trans-L-1,2-cyclohexanediamine with M2PtX4 (M = Li, Na, K, X = I, Cl, Br) and KI at room temperature and purification by suspending the solid in an appropriate solvent. The present invention is further related to the preparation of highly pure oxaliplatin by reacting the cis-diiodo(trans-l-1,2-cyclohexanediamine)platinum(II) with silver oxalate and subsequently with KX (X = Cl, Br, I) followed by purification Oxaliplatin is also prepared via reaction of cis-diaqua(trans-l-1,2-cyclohexanediamine)platinum(II) (obtained by treating the diiodo complex with AgNO3) with potassium oxalate.

L6 ANSWER 7 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:47518 CAPLUS
DN 144:120211
TI Synthesis of oxaliplatin
IN Pu, Shaoping; Yu, Yao; Wang, Yutian; Gao, Wengui; Liu, Zhudong
PA Kunming Institute of Precious Metals, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1634945	A	20050706	CN 2004-10079552	20041108
PRAI CN 2004-10079552		20041108		

OS CASREACT 144:120211
AB The process comprises allowing to react cis-diiodo(trans-(-)-1,2-cyclohexanediamino)platinum(II) with AgNO3 solution in dark ambient at 30-80° for 4-10 h, filtering, and then allowing to react the filtrate with K2C2O4 for 2-7 h.

L6 ANSWER 8 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1119444 CAPLUS
DN 144:31640
TI Synthesis and structure-activity relationships of mono- and dialkyl-substituted oxaliplatin derivatives
AU Habala, Ladislav; Galanski, Markus; Yasemi, Afshin; Nazarov, Alexey A.; von Keyserlingk, Nikolai Graf; Keppler, Bernhard K.
CS Institute of Inorganic Chemistry - Bioinorganic, Environmental- and Radiochemistry, University of Vienna, Vienna, A-1090, Austria
SO European Journal of Medicinal Chemistry (2005), 40(11), 1149-1155
CODEN: EJMCA5; ISSN: 0223-5234
PB Elsevier Ltd.
DT Journal
LA English
OS CASREACT 144:31640
AB To improve the pharmacol. profile of the anticancer drug oxaliplatin, (trans-R,R-cyclohexane-1,2-diamine)oxalatoplatinum(II), and to explore activity-structure relations, new mono- and dialkyl substituted oxaliplatin analogs were synthesized. Following a new synthetic strategy, racemates with a defined stereochem. at C atoms 1, 2, 4, and 5 of the cyclohexane ring could be prepared, which is the basis for reliable structure-activity relations and the following enantiomer resolution The cytotoxicity was evaluated in nine tumor cell lines, indicating that bulky substituents have a neg. influence on the cytotoxic potency of the

oxaliplatin derivs. With respect to the antiproliferative properties, the 4-methyl-, cis-4,5-dimethyl-, and especially the 4,4-dimethyl-trans-cyclohexane-1,2-diamine(oxalato)platinum(II) complexes are the most promising candidates to be further evaluated.

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:823717 CAPLUS
DN 143:221342
TI An improved process for the preparation platinum(II) 1,2-cyclohexanediamine dicarboxylato complexes for use as anti-tumor agents
IN Maikap, Golak Chandra; Raj, Bhagat; Kumar, Pradipta; Vivekanandan, Kannan; Belwal, Chandrakant
PA Dabur Research Foundation, India
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005075489	A1	20050818	WO 2004-IN35	20040205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1749015	A1	20070207	EP 2004-708433	20040205
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PT, RO, SE, SI, SK, TR				
IN 2004DN00374	A	20060310	IN 2004-DN374	20040220
PRAI WO 2004-IN35	W	20040205		

OS CASREACT 143:221342; MARPAT 143:221342
AB Platinum complexes cis-[Q1(NH2)2Pt(O2C)2Q2] [Q1(NH2)2 = cis-, (R,R)-trans-, (S,S)-trans-1,2-cyclohexanediamine; Q2 = cyclo-C(CH2)n, (CH2)n, R3-(un)substituted o-phenylene, n = 0-5, R3 = H, alkoxy, halo, NO2] useful as relatively non-toxic carcinostatic agents (no data), were prepared by reaction of potassium tetrachloroplatinate with Ag2Y (Y = CO3, O; preferably Y = O) in the presence of dicarboxylic acid Q2(CO2H), preferably oxalic acid and cyclohexanediamine or by reaction of cis-[Q1(NH2)2PtX2] (X = carboxylato, sulfonato; preferably X = AcO-, MeSO3-) with alkali metal dicarboxylate, preferably with dipotassium oxalate; the improved process provides high yields of the title complexes and low content of impurities. In an example, cis-[(R,R)-1,2-cyclohexanediamine]diiodoplatinum (1) was prepared by reaction of 0.24 mol of KI and 0.06 mol of K2PtCl4 in 1.5 L of water at 30° for 30 min., followed by addition of 0.06 mol of (R,R)-1,2-cyclohexanediamine; the dichloro-analog cis-[(R,R)-1,2-cyclohexanediamine]dichloroplatinum (2) was prepared in a similar way by reaction of K2PtCl4 and (R,R)-1,2-cyclohexanediamine. The target cis-[(R,R)-1,2-cyclohexanediamine][oxalato(2-)]platinum (Oxaliplatin) was prepared from 1 (0.07 mol) by reaction with 0.07 mol of Ag2O and 0.06 mol of oxalic acid dihydrate; the process does not require addnl. treatment with KI for removal of the remaining silver salts. In other examples, Oxaliplatin was prepared by converting of 2 into cis-bis-acetato or cis-bis-methanesulfonato complexes with subsequent reaction with dipotassium oxalate.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:725943 CAPLUS
DN 143:185695
TI Process for preparing 1,2-diaminocyclohexane-platinum(II) carboxylate complexes
IN Pepels, Andreas; Schnebeck, Ralf-Dieter; Rauter, Holger; Wissmann, Friedrich
PA W. C. Heraeus G.m.b.H., Germany
SO Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1561754	A1	20050810	EP 2005-774	20050115
	EP 1561754	B1	20070307		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
	DE 102004005906	B3	20050929	DE 2004-102004005906	20040205
	CA 2492254	A1	20050805	CA 2005-2492254	20050111
	AT 356136	T	20070315	AT 2005-774	20050115
	AU 2005200417	A1	20050825	AU 2005-200417	20050201
	US 2005197389	A1	20050908	US 2005-50382	20050203
	BR 2005000307	A	20051108	BR 2005-307	20050203
	CN 1680411	A	20051012	CN 2005-10008330	20050205
	JP 2005220138	A	20050818	JP 2005-31078	20050207
	IN 2005CH00102	A	20070316	IN 2005-CH102	20050207
PRAI	DE 2004-102004005906	A	20040205		

OS CASREACT 143:185695; MARPAT 143:185695
AB The process for the preparation of PtL(C2O4) (L = trans-1,2-cyclohexanediamine) in 80 % yield involves the reaction of K2PtCl4 with KI followed by reaction with L to give PtLI2. Aquation of PtLI2 gave PtL(H2O)22+ which was then reaction with (NH4)2C2O4.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:547232 CAPLUS
DN 143:65482
TI Prodrug compositions including amino acids
IN Hilfinger, John
PA USA
SO U.S. Pat. Appl. Publ., 14 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005137141	A1	20050623	US 2004-972729	20041025
PRAI	US 2003-514121P	P	20031024		

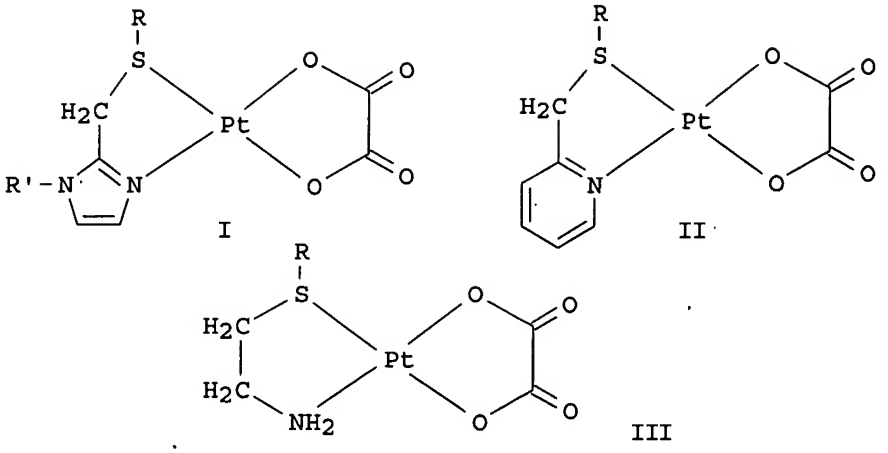
AB A prodrug composition is provided which includes a pharmaceutical species and an amino acid having a covalent bond to the pharmaceutical species. The pharmaceutical species is characterized by bioavailability of 30% or less and a mol. weight in the range of 100 to 1000 Daltons. The composition is characterized further in that the pharmaceutical species is not acyclovir, ganciclovir, BRL44385, or penciclovir. Also described is an inventive method of delivering a pharmaceutical species to an individual including the step of orally administering an inventive prodrug to an individual. In one embodiment the prodrug includes a pharmaceutical species

characterized by bioavailability of 30% or less, wherein the pharmaceutical species has a mol. weight in the range of 100 to 1000 Daltons. The inventive prodrug is transported from the gastrointestinal lumen by a specific transporter and is enzymically cleaved to yield the pharmaceutical species, such that the pharmaceutical species is delivered to the individual. Thus, 3'-monoester, 5'-monoester, and 3',5'-diester prodrugs of floxuridine were synthesized by reaction of 1.8 mmole of N-tert-Boc-amino acid (Phe, Val, Asp, and Lys) and 1.33 mmole of floxuridine in the presence of dimethylpyrindin-4-ylamine and dicyclohexylcarbodiimide in DMF. The solution was stirred under a nitrogen atmospheric at ambient temperature for 48 h, the mixture was filtered, the DMF was removed from the filtrate, and the residue was chromatographed on silica gel. After evaporation of the desired fractions, the resulting white solid intermediate was dissolved in trifluoroacetic acid/CH2Cl2 (1:1) and stirred at 0° for 30 min. The excess acid was removed in vacuo. The residue was freeze-dried to obtain the desired prodrug as a hygroscopic, fluffy white solid. For each amino acid, three prodrugs were synthesized: a 5'-ester, a 3'-ester and a 5',3'-diester.

L6 ANSWER 12 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:493614 CAPLUS
DN 143:37556
TI Preparation of platinum(II) dicarboxylate complexes for use as antitumor agents
IN Du Preez, Jan Gysbert Hermanus
PA Platco Technologies Proprietary Limited, S. Afr.
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005051966	A1	20050609	WO 2004-IB3855	20041124
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2547275	A1	20050609	CA 2004-2547275	20041124
	EP 1704156	A1	20060927	EP 2004-798964	20041124
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
PRAI	US 2003-524727P	P	20031125		
	WO 2004-IB3855	W	20041124		

OS CASREACT 143:37556
GI



I II III

AB This invention relates to a method for the preparation of platinum(II) complexes, in particular dicarboxylatoplatinum(II) complexes containing a neutral bidentate ligand, such as oxaliplatin. The method includes the step of reacting a bis(dicarboxylato)platinate(II) species with a suitable neutral bidentate ligand to form a neutral dicarboxylatoplatinum(II) complex and, if necessary, recrystg. the product to form a pure dicarboxylatoplatinum(II) complex containing a neutral bidentate ligand. The invention also relates to a method for producing a bis-dicarboxylatoplatinate(II) species, and to new platinum(II) complexes that can be made by the method of the invention. Thus, platinum(II) oxalato complexes (I; R = Me, Bu; R' = Et, Pr, Me and II; R = Me, Et, Pr and III; R = Me, Et, Pr) were prepare and complex I (R = Me, R' = Pr) was tested for antitumor activity.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:479362 CAPLUS
DN 143:120485
TI Preparation of oxaliplatin
IN Pu, Shaoping; Gao, Guigui; Liu, Zhudong
PA Institute of Precious Metals, Kunming, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1521161	A	20040818	CN 2003-103908	20030130
PRAI	CN 2003-103908		20030130		

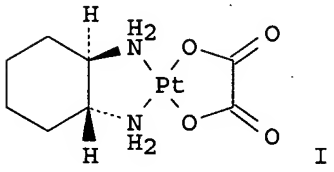
AB The present invention is the preparation process of antitumor medicine Oxaliplatin C8H14N2O4Pt. In the technol. process, cis-dichloro cyclohexanediamine-platinum (II) or cis-diiodo cyclohexanediamine-platinum (II) as initiator is made to react with silver oxalate in lucifugous condition at 40-75°c to obtain water solution of Oxaliplatin; and the water solution is further decompression concentrated to obtain solid Oxaliplatin product. The said Oxaliplatin preparation process is short, high in production efficiency and easy in operation.

L6 ANSWER 14 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:348666 CAPLUS
DN 143:216557
TI Process for producing oxaliplatin

IN Zak, Frantisek; Svehla, Pavel; Mikolin, Petr
PA Pliva Lachema A. S., Czech Rep.
SO Czech Rep., 7 pp.
CODEN: CZXXED
DT Patent
LA Czech
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CZ 294668	B6	20050216	CZ 2001-4409	20011210
PRAI	CZ 2001-4409		20011210		

GI



I

AB The present invention relates to a process for producing oxaliplatin, i.e. a metallopharmaceutical exhibiting antineoplastic activity, which is chemical represented by (SP-4-2)-[(1R,2R)-1,2-cyclohexandiamine-N,N']-(oxalato-O,O')-platinum complex of general formula (I).

L6 ANSWER 15 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:347023 CAPLUS
DN 142:384533
TI Improved process for preparation of antitumor agent oxaliplatin with a low content of accompanying impurities of silver, alkali metals and nitrates
IN Zak, Frantisek; Czajka-Poulova, Anna
PA Pliva-Lachema A.S., Czech Rep.
SO PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005035544	A1	20050421	WO 2004-CZ68	20041014
	WO 2005035544	A8	20050909		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CZ 297703	B6	20070307	CZ 2003-2855	20031017
	CA 2540374	A1	20050421	CA 2004-2540374	20041014
	EP 1680434	A1	20060719	EP 2004-762320	20041014
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR				
	CN 1867574	A	20061122	CN 2004-80029942	20041014
	US 2007073074	A1	20070329	US 2006-595286	20060405
PRAI	CZ 2003-2855	A	20031017		
	WO 2004-CZ68	W	20041014		

AB Oxaliplatin, [(1R,2R)-cyclohexanediamine-N,N'][oxalato(2-)]platinum (1), useful as antitumor agent active against colon and rectum malignant tumors (no data) was prepared in pure form containing, by weight, at most 0.01 %, preferably less than 0.001 %, of alkali metals, at most 0.0005 %, preferably less than 0.0002 %, of silver, and at most 0.01 %, preferably less than 0.001 %, of nitrates, by room-temperature reaction of the suspension of dichloro[(1R,2R)-cyclohexanediamine-N,N']platinum with silver nitrate in 1:2 ratio, preferably with 1 mol% excess of AgNO3, followed by treatment with ammonium iodide RR1R2R3NI [R = (un)substituted C1-10 alkyl, (un)substituted C3-10 cycloalkyl; same R1, R2, R3, or R1, R2, R3 = H]; the reaction of the resulting aqueous solution with oxalic acid and recrystn. of the product 1 from water, washing with polar organic solvent, preferably ethanol. The invented method does not include any reactions with alkali metal salts, which lowers their concentration in the product. In an example, 80.6 g of AgNO3 was added to a suspension of 88.9 g of dichloro[(1R,2R)-cyclohexanediamine-N,N']platinum in 900 mL of water, stirred 70 h at room temperature in the absence of light; after removal of the solids the filtrate was treated with 2,5 g of Et4NI and 0.6 g of activated charcoal. The solution was then reacted with 29.5 g of oxalic acid dihydrate for 4 h, the precipitated oxaliplatin 1 was filtered, dried, recrystd. from water and washed with 30 mL of water and 400 mL of ethanol, affording 50.2 g of 1 (54% yield). The obtained sample of 1 contained <0.001 wt% of alkali metals, <0.0002 wt% of silver, <0.001 wt% of nitrates and <0.01 wt% of oxalic acid.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:283530 CAPLUS
DN 142:355781
TI Multi-arm polymer prodrugs
IN Zhao, Xuan; Bentley, Michael D.; Ren, Zhongxu; Viegas, Tacey X.
PA Nektar Therapeutics Al, Corporation, USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005028539	A2	20050331	WO 2004-US30720	20040917
	WO 2005028539	A3	20051124		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2004274489	A1	20050331	AU 2004-274489	20040917
	CA 2537336	A1	20050331	CA 2004-2537336	20040917
	US 2005112088	A1	20050526	US 2004-943799	20040917
	EP 1675622	A2	20060705	EP 2004-784560	20040917
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
	BR 2004014017	A	20060905	BR 2004-14017	20040917
	CN 1852740	A	20061025	CN 2004-80026809	20040917
	JP 2007505928	T	20070315	JP 2006-527105	20040917

PRAI US 2003-503673P P 20030917
US 2004-584308P P 20040630
WO 2004-US30720 W 20040917

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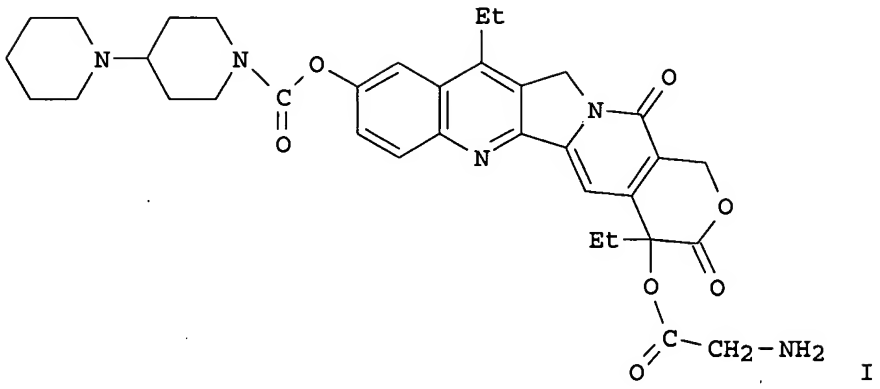


I

AB The prodrugs of the invention comprise a water-soluble polymer having three or more arms, at least three of which are covalently attached to an active agent, e.g., a small mol. The conjugates of the invention provided an optimal balance of polymer size and structure for achieving improved drug loading, since the conjugates of the invention possess three or more active agents releasably attached to a multi-armed water soluble polymer. The prodrugs of the invention are therapeutically effective, and exhibit improved properties in-vivo when compared to unmodified parent drug. A typical prodrug was manufactured by stirring a CH2Cl2 solution containing glycine-irinotecan I 0.516, pentaerythritol tetrakis(polyethylene glycol monocarboxymethyl ether) 3.904, 2-hydroxybenzyltriazole 0.0658, and dicyclohexylcarbodiimide 0.282 g overnight.

L6 ANSWER 17 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:127964 CAPLUS
DN 142:360733
TI Purification of oxaliplatin
IN Pu, Shaoping; Liu, Zhudong; Gao, Wengui; Yu, Yao; Wang, Yutian; Liu, Yang; Liu, Weiping; He, Jian; Chen, Xizhu
PA Kunming Institute of Nobel Metal, Peop. Rep. China
SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 5 pp.
CODEN: CNXXEV
DT Patent
LA Chinese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CN 1460683	A	20031210	CN 2003-135146	20030606
PRAI CN 2003-135146		20030606		

AB The process comprises dissolving oxaliplatin in 40-90° water, precipitating Ag+ with KI, and vacuum concentrating

L6 ANSWER 18 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:31665 CAPLUS
DN 142:290597
TI Cytotoxicity of cis-Platinum(II) Conjugate Models. The Effect of Chelating Arms and Leaving Groups on Cytotoxicity: A Quantitative Structure-Activity Relationship Approach
AU Monti, Elena; Gariboldi, Marzia; Maiocchi, Alessandro; Marengo, Emilio; Cassino, Claudio; Gabano, Elisabetta; Osella, Domenico
CS Dipartimento di Biologia Strutturale e Funzionale, Universita

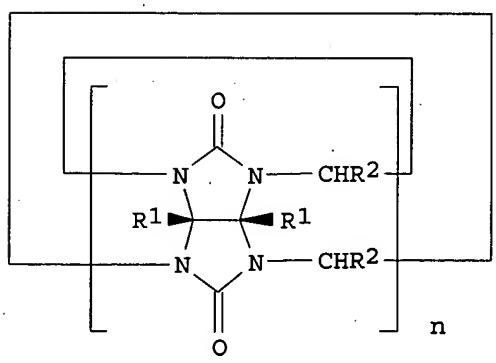
dell'Insubria, Busto Arsizio, 21052, Italy
SO Journal of Medicinal Chemistry (2005), 48(3), 857-866
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Thirteen newly synthesized or resynthesized diamine-platinum(II) complexes were characterized, and their cytotoxic activities (IC50) were tested on parental and resistant ovarian cancer cell lines. They represent models of conjugates between biol. active vectors and cytotoxic PtII moieties within the "drug targeting and delivery strategy". Three drugs, routinely employed in the clin. treatment of cancer, namely, cisplatin, carboplatin, and oxaliplatin, were also included in the study as controls. The quant. structure-activity relationship approach provides simple regression models able to predict log(1/IC50) of diamine-platinum(II) complexes on both parental and resistant ovarian cancer cell lines. The 16 complexes were characterized using 197 mol. descriptors, after which the best regression models relating a subset of these descriptors to the log(1/IC50) in the two cancer cell lines were calculated Models with four variables proved to be endowed with very good predictive ability Q2LMO-50% ≥ 85.6%, making it possible to discard 50% of the mols. from the test set following for cross-validation procedure. A four-variable regression model also proved effective in predicting the resistance index RI, Q2LMO-50% = 84.4%.
RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:445270 CAPLUS
DN 139:357356
TI Chiral palladium(II) and platinum(II) complexes of diaminocyclohexane: X-ray structures of (1R,2R)-(-)-1,2-diaminocyclohexane dihydrochloride and its corresponding oxalato platinum(II) complex
AU Abu-Surrah, Adnan S.; Al-Allaf, Talal A. K.; Klinga, Martti; Ahlgren, Markku
CS Department of Chemistry, Hashemite University, Zarqa, 13115, Jordan
SO Polyhedron (2003), 22(12), 1529-1534
CODEN: PLYHDE; ISSN: 0277-5387
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 139:357356
AB The nucleophilic substitution reaction of the enantiomerically pure ligand, (1R,2R)-(-)-1,2-diaminocyclohexane [DACH] (1) with cis-bis(benzonitrile)palladium(II) dichloride [(PhCN)2PdCl2] gives [(DACH)PdCl2] (2) in a high yield. The reaction of the corresponding platinum(II) complex [(PhCN)2PtCl2] with DACH, under the same reaction conditions, surprisingly, took a different course, in which nucleophilic addition to the benzonitrile ligand occurred forming an enantiomerically pure amidine complex [(PhC:NH-NH(C6H10)NH2)Pt(N.tplbond.CPh)Cl]Cl (3), where the nitrogen ligand form a seven-membered chelate around the central atom. The aqua and oxalato derivs. of complex 2, [(DACH)Pd(H2O)2](NO3)2 (4) and [(DACH)Pd(C2O4)] (5) also were prepared and characterized. The platinum analog complex to 5, [(DACH)Pt(C2O4)] (6), was prepared starting from the enantiomerically pure isomer (1) and the platinum salt K2PtX4 (X = Cl, I). According to x-ray structural anal. carried out on the complex, the product does not consist of just the desired isomer, but a mixture of both the trans-l (trans-(-)-1R,2R) and trans-d (trans-(+)-1S,2S) isomers. No retention of optical isomerism was observed The single crystal structural anal. was also carried out on the ligand (1R,2R)-(-)-diaminocyclohexane dihydrochloride (DACH·2HCl) (1a). The result indicates, however, that only the R,R-isomer exists in the free ligand.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

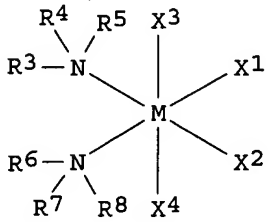
L6 ANSWER 20 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:242344 CAPLUS
DN 138:264767
TI Inclusion compounds comprising host cucurbituril derivatives and guest metal complexes and their pharmaceutical compositions for treatment of cancer
IN Kim, Kimoon; Jeon, Young Jin; Kim, Soo-Young; Ko, Young Ho
PA Postech Foundation, S. Korea
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003024978	A1	20030327	WO 2002-KR1755	20020918
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	KR 2003024426	A	20030326	KR 2001-57573	20010918
	EP 1430061	A1	20040623	EP 2002-765666	20020918
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	JP 2005503415	T	20050203	JP 2003-528825	20020918
	US 2004265237	A1	20041230	US 2004-489968	20040318
PRAI	KR 2001-57573	A	20010918		
	WO 2002-KR1755	W	20020918		

OS MARPAT 138:264767
GI



I



II

AB The present invention provides an inclusion compound having a variety of cucurbituril derivs. I, e.g., cucurbitu[7]ril, as a host mol. and metal complexes II (representing a wide variety of complexes), and especially platinum complexes, e.g., oxaliplatin, as a guest mol. A pharmaceutical composition having an anticancer effect can be obtained by using the inclusion compound according to the present invention. The pharmaceutical composition can prevent effective components from being biol. degraded in vivo and can exhibit

continuous drug effect for a long time, just by a single dosage, by controlling the release time of the Pt complex once it reaches target tumor cells. The inclusion compound is used for treatment of cancer, including ovarian cancer, breast cancer, or colon cancer. Antiproliferative activities are reported of oxaliplatin-cucurbitu[7]ril 1:1 inclusion compound against A 549 (human non-small lung), SKOV-3 (human ovarian), SKMEL-2 (human melanoma), XF-498 (human CNS), and HCT-15 (human colon).

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:42282 CAPLUS
DN 138:99961
TI Oxaliplatin active substance with a very low content of oxalic acid
IN Ibrahim, Houssam
PA Debiopharm S.A., Switz.
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003004505	A1	20030116	WO 2002-CH358	20020702
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1404689	A1	20040407	EP 2002-734974	20020702
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	DE 20221678	U1	20061228	DE 2002-20221678	20020702
	US 2004186172	A1	20040923	US 2003-482367	20031230
PRAI	WO 2001-CH414	W	20010702		
	WO 2001-CH618	W	20011015		
	EP 2002-734974	A	20020702		
	WO 2002-CH358	W	20020702		

AB The present invention relates to an oxaliplatin active substance for a pharmaceutical composition, wherein its weight content in oxalic acid is ≤0.08 %, and to a process of preparing the active substance. Oxaliplatin, cis-(trans-l-1,2-diaminocyclohexane)(oxalato)platinum, was prepared by the reaction of K2PtCl4 with trans-l-1,2-diaminocyclohexane (L) to give [PtLCl2] which was teated with aqueous AgNO3 to give [PtL(OH2)2]2+. This latter complex was treated with a catalytic amount of KI or NaI and active C and subsequently treated with M2C2O4 (M = Li, Na, K). Cis-(trans-l-1,2-diaminocyclohexane)(oxalato)platinum was used in a pharmaceutical composition in the form of a lyophilisate as the active substance. The toxicity of cis-(trans-l-1,2-diaminocyclohexane)(oxalato)platinum was established.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 22 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2002:280369 CAPLUS
DN 137:379724
TI Synthesis and cytotoxicity of the dihydrated complex of oxaliplatin
AU Videhult, Pernilla; Yachnin, Jeffrey; Jerremalm, Elin; Lewensohn, Rolf; Ehrsson, Hans

CS Karolinska Pharmacy, Karolinska Hospital, Stockholm, SE-171 76, Swed.
SO Cancer Letters (Shannon, Ireland) (2002), 180(2), 191-194
CODEN: CALEDQ; ISSN: 0304-3835
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB A new way of synthesizing the dihydrated oxaliplatin complex (DOC) is presented and its cytotoxicity is compared to that of oxaliplatin and cisplatin. By hydrolyzing oxaliplatin in aqueous sodium hydroxide at 70, DOC was formed in less than 1 h. Cytotoxicity was studied in the non-small cell lung cancer cell line A549 using the fluorescent microculture cytotoxic assay. Oxaliplatin and cisplatin had similar cytotoxicity profiles, whereas DOC was considerably more toxic. The cytotoxicity of oxaliplatin might, at least in part, be mediated through the formation of DOC.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 23 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2000:281268 CAPLUS
DN 133:12057
TI Synthesis and characterization of oxaliplatin
AU Pu, Shaoping; Yang, Yikun; Gao, Wengui; Yu, Yao; Liu, Weiping
CS Kunming Institute of Precious Metals, Kunming, 650221, Peop. Rep. China
SO Guijinshu (2000), 21(1), 26-27
CODEN: GUIJE7; ISSN: 1004-0676
PB Guijinshu Jikan Bianjibu
DT Journal
LA Chinese
AB A new synthesis process with good stability and high yield for production of cis-oxalato(trans-(R,R)-(-)1,2-cyclohexanediamine)platinum(II) (oxaliplatin) was introduced. The chemical structure of oxaliplatin was identified by using elemental anal. as well as IR, MS, UV and 1H NMR spectroscopy etc.

L6 ANSWER 24 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1999:191779 CAPLUS
DN 130:347020
TI A new orally active antitumor 1R,2R-cyclohexanediamine-platinum(IV) complex. Trans-(n-valerato)chloro(1R,2R-cyclohexanediamine)(oxalato)platinum(IV)
AU Kizu, Ryoichi; Nakanishi, Takeo; Hayakawa, Kazuichi; Matsuzawa, Akio; Eriguchi, Masazumi; Takeda, Yasutaka; Akiyama, Nachio; Tashiro, Tazuko; Kidani, Yoshinori
CS Fac. Pharmaceutical Sciences, Kanazawa Univ., Kanazawa, 920, Japan
SO Cancer Chemotherapy and Pharmacology (1999), 43(2), 97-105
CODEN: CCPHDZ; ISSN: 0344-5704
PB Springer-Verlag
DT Journal
LA English
AB Trans-(n-alkanoato)chloro(1R,2R-cyclohexanediamine)(oxalato) platinum(IV) (Cn-OHP-Cl) complexes with the n-alkanoate ligand being butyrate, valerate, caproate, or heptanoate were synthesized and tested for their antitumor activity in i.p. L1210 murine leukemia and s.c. implanted murine reticulosarcoma M5076 models. The valerate complex (C5-OHP-Cl) was the most effective in the leukemia model and also orally active in the reticulosarcoma model, whereas the corresponding trans-bis(n-valerato)(1R,2R-cyclohexanediamine)(oxalato)platinum(IV) was not. The enhanced activity of C5-OHP-Cl is considered to be due in part to increased susceptibility to reduction and increased gastrointestinal absorption as is indicated by more rapid in vitro reduction by ascorbate and by higher plasma levels of total and filtrable Pt, resp.
RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 25 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1998:331281 CAPLUS
DN 129:62007
TI Synthesis of [3H2]-(R,R)-1,2-Diaminocyclohexaneoxalatoplatinum(II), [3H2]-Oxaliplatin
AU Burgos, Alain; Ellames, George J.
CS Isotope Chemistry Laboratories, Department of Preclinical Metabolism and Pharmacokinetics, Sanofi Research, Alnwick Research Centre, Alnwick, NE66 2JH, UK
SO Journal of Labelled Compounds & Radiopharmaceuticals (1998), 41(5), 443-449
CODEN: JLCRD4; ISSN: 0362-4803
PB John Wiley & Sons Ltd.
DT Journal
LA English
AB A synthesis of [3H2]-(R,R)-1,2-diaminocyclohexaneoxalatoplatinum(II), [3H2]-Oxaliplatin, (2), is described. Rac-trans-4-Cyclohexene-1,2-dicarboxylic acid di-Et ester, (6), was converted to rac-trans-1,2-diaminocyclohex-4-ene, (7), by modification of known chemical aimed at avoiding reported hazards. Resolution of the diamine, (7), with L-(+)-tartaric acid afforded the (R,R)-1,2-diaminocyclohex-4-ene, (8), which was converted to the (R,R)-1,2-bis(tert-butoxy-carbamino)cyclohex-4-ene, (10), and tritiated to yield [3H2]-(R,R)-1,2-bis(tert-butoxycarbamino)-cyclohexane, (11). Hydrolysis of 11 afforded [3H2]-(R,R)-1,2-diaminocyclohexane, (12), which was converted to the desired [3H2]-(R,R)-1,2-diaminocyclohexaneoxalatoplatinum(II), [3H2]-Oxaliplatin, 2.
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 26 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:682245 CAPLUS
DN 127:302489
TI Process of preparing platinum cyclohexanediamine oxalate complexes of high purity
IN Taniuchi, Jun-ichi; Nakanishi, Chihiro; Ohnishi, Yuko
PA Tanaka Kikinzoku Kogyo K.K., Japan; Dediopharm S.A.
SO Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 801070	A2	19971015	EP 1996-830537	19961018
	EP 801070	A3	19980826		
	EP 801070	B1	20030416		
	R: BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT				
	JP 09278785	A	19971028	JP 1996-86954	19960410
	JP 10017587	A	19980120	JP 1996-174788	19960704
	JP 3154399	B2	20010409		
	EP 1308453	A2	20030507	EP 2003-861	19961018
	EP 1308453	A3	20030514		
	R: BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT				
	EP 1308454	A2	20030507	EP 2003-863	19961018
	EP 1308454	A3	20030514		
	EP 1308454	B1	20050601		
	R: BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, PT				
	PT 801070	T	20030731	PT 1996-830537	19961018
	ES 2194967	T3	20031201	ES 1996-830537	19961018
	PT 1308454	T	20050930	PT 2003-863	19961018
	ES 2243807	T3	20051201	ES 2003-863	19961018
	WO 9801454	A1	19980115	WO 1997-JP2332	19970704

W: US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

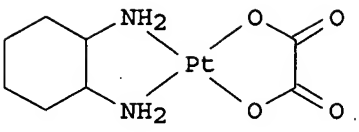
	EP 881226	A1	19981202	EP 1997-929532	19970704
	EP 881226	B1	20031126		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	AT 255118	T	20031215	AT 1997-929532	19970704
	PT 881226	T	20040331	PT 1997-929532	19970704
	ES 2210543	T3	20040701	ES 1997-929532	19970704
	US 5959133	A	19990928	US 1998-29682	19980303
PRAI	JP 1996-86954	A	19960410		
	JP 1996-174788	A	19960704		
	EP 1996-830537	A3	19961018		
	WO 1997-JP2332	W	19970704		

OS MARPAT 127:302489
GI For diagram(s), see printed CA Issue.
AB Disclosed are processes for the preparation of platinum cyclohexanediamine oxalate complexes I (R = oxalate, oxalate derivative) with elevated yield and preventing contamination with impurities. Reaction of cis-[diaqua(trans-l-1,2-cyclohexanediamine)platinum(II)] with oxalic acid or oxalate derivative where the pH is adjusted to 3.0-6.0 with an alkali solution, e.g., KOH, affords I (R = oxalate, oxalate derivative). Reaction of a cis-platinum(II) 1,2-cyclohexanediamine dihalo complex (diamine ligand is cis, trans-l or trans-d, halo is Cl or Br) with 2.01-2.1 molar equiv silver ion solution, removing the silver halide produced, adding NaI or KI and active carbon, filtering out impurities, followed by addition of an organic dibasic acid to the filtrate gives oxalate complexes I. The preparation of complexes I starting from potassium or sodium tetrachloroplatinate and the cyclohexanediamine are performed under ≤ 5% O2, or under N2, in vacuo or in an inert gas atmospheric in deoxygenated water. Thus, for elevating a yield of I and preventing the contamination of impurities, the pH of a solution and an amount of a Ag ion are adjusted, and a reaction environment is so controlled that oxidation is difficult to occur.

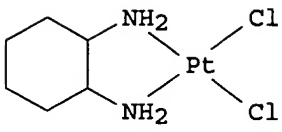
L6 ANSWER 27 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:449012 CAPLUS
DN 127:75097
TI Preparation of oxalato[trans-(-)-1,2-cyclohexanediamine]platinum(II) as an anticancer agent
IN Yanai, Junichi
PA Tanaka Kikinzoku Kogyo K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 09132583	A	19970520	JP 1995-292760	19951110
PRAI	JP 1995-292760		19951110		

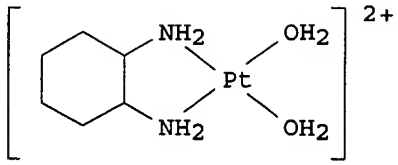
GI



I



II



$(NO_3^-)_2$ III

AB White crystalline title compound (I), useful as an anticancer agent (no data), is
prepared by treating trans-(-)-1,2-cyclohexanediamine with dipotassium tetrachloroplatinate in H2O at room temperature for ≥10 h, dispersing yellow needle-shaped crystalline dichloro[trans-(-)-1,2-cyclohexanediamine]platinum(II) (II) into H2O, treating with 2-fold mol. amount of AgNO3, removing AgCl by filtration, treating with KI for ≥12 h to precipitate unreacted Ag ion, decolorizing with activated C, treating with (CO2H)2.2H2O for 4-100 h, and recrystg. from hot water. Trans-(-)-1,2-cyclohexanediamine was treated with dipotassium tetrachloroplatinate in H2O at room temperature for ≥10 h to give 99% II. This was treated with AgNO3 in H2O under dark for ≥24 h and treated with KI for removing excess Ag+ ions for ≥12 h to give an aqueous solution containing diaquo[trans-(-)-1,2-cyclohexanediamine]platinum(II) nitrate (III) which was reacted with (CO2H)2.2H2O for 48 h, and recrystd. from H2O to give 55% I.

L6 ANSWER 28 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1997:250171 CAPLUS
DN 126:232711
TI Manufacture of high-purity cyclohexanediamine platinum complex for antitumor agent
IN Yanai, Junichi; Nakanishi, Chihiro
PA Tanaka Precious Metal Ind, Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 09040685	A	19970210	JP 1995-209149	19950725
	JP 3022264	B2	20000315		
	CN 1150587	A	19970528	CN 1996-111312	19960725
	CN 1067400	B	20010620		
	CN 1422860	A	20030611	CN 2000-135215	20001128
PRAI	JP 1995-209149	A	19950725		
	JP 1996-86954	A	19960410		

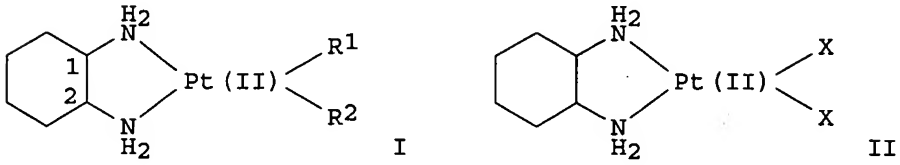
AB PtL2Q (I; L = 1-trans-1,2-cyclohexanediamine; H2Q = HO2CCO2H, HO2CRCO2H (R = CH2, CHMe, 1,1-cyclobutanediyl, 4-carboxy-1,2-phenylene), HO2CCH2OH) are manufactured by treating PtL(H2O)2 with H2Q with control of pH to 3.0-6.0 by addition of an alkali solution I with high purity was obtained with high yield.

L6 ANSWER 29 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN

AN 1995:884008 CAPLUS
DN 123:305193
TI preparation of cyclohexanediamine-platinum complexes in high purity
IN Oonishi, Hiroko
PA Tanaka Precious Metal Ind, Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 07025890	A	19950127	JP 1993-194283	19930709
PRAI	JP 1993-194283		19930709		

OS MARPAT 123:305193
GI



AB The title complexes [I; R1R2 = dibasic acid residue such as oxalyl, malonyl, etc.], useful as anticancer agents (no data), are prepared in high purity by reaction of dihalo complexes II (X = Br, Cl) with dibasic acids at pH 1.0-2.0. Reaction of trans-1,2-diaminocyclohexane with K2PtCl6 in H2O gave trans-II (X = Cl), which was treated with aqueous AgNO3 at room temperature, the filtrate was concentrated and treated with KI, the iodide ppts. were filtered, the filtrate was adjusted to pH 7.0 with 2N NaOH and filtered again, the filtrate was acidified to pH 2.0 with 2N HNO3 and then treated with aqueous oxalic acid to give 60% 1,2-trans-I (R1R2 = oxalyl) containing < 5 ppm Cl- or I-, vs. a brownish-yellow impure product without the acidification process.

L6 ANSWER 30 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1995:459501 CAPLUS
DN 122:329198
TI Process for preparing optically pure cis-oxalato(trans-l-1,2-cyclohexanediamine) Pt(II) complex
IN Okamoto, Koji; Nakanishi, Chihiro; Taniushi, Junichi; Ohnishi, Junji; Komoda, Yasunibu
PA Tanaka Kikinzoku Kogyo K.K., Japan
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 625523	A1	19941123	EP 1993-830384	19930916
	EP 625523	B1	20011031		
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
	JP 06329692	A	19941129	JP 1993-142824	19930521
	JP 3025602	B2	20000327		
	US 5420319	A	19950530	US 1993-117892	19930907
	ES 2167328	T3	20020516	ES 1993-830384	19930916
PRAI	JP 1993-142824	A	19930521		

AB Anticancer cis-oxalato(trans-l-1,2-cyclohexanediamine) Pt(II) with an

optical purity ≥ 99.94% is prepared from optically pure trans-l-1,2-cyclohexanediamine or an optically pure trans-l-1,2-cyclohexanediamine derivative The starting material was optically resolved by HPLC using a column packed with a chiral filler.

L6 ANSWER 31 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1995:259901 CAPLUS
DN 122:45003
TI Platinum compound and process of preparing same.
IN Okamoto, Koji; Hoshi, Yuko; Nakanishi, Chihiro
PA Tanaka Kikinzoku Kogyo K.K., Japan
SO Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 617043	A1	19940928	EP 1993-830118	19930325
	EP 617043	B1	20011031		
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
	JP 05194332	A	19930803	JP 1992-23219	19920113
	JP 07076230	B	19950816		
	ES 2166760	T3	20020501	ES 1993-830118	19930325
PRAI	JP 1992-23219		19920113		
	EP 1993-830118	A	19930325		

AB Disclosed herein are a Pt compound employed as raw material of medicines having carcinostatic effects, and a process of preparing the Pt compound The Pt compds. PtLL' (L = 1,2-cyclohexanediamine isomer, L' = OC(O)CH2O, OC(O)C(O)O or OC(O)RC(O)O (R = CH2, CHMe, cyclo-Bu,, C6H3CO2H)) can be prepared substantially free from impurities through a reaction between the corresponding dihalogen compound and an organic dibasic acid employing differences of solubilities. As an example, PtLL' (L = trans-1,2-cyclohexanediamine, L = OC(O)C(O)O) is prepared No antitumor data are reported.

L6 ANSWER 32 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:337782 CAPLUS
DN 120:337782
TI preparation of platinum complexes
IN Nakanishi, Chihiro; Yanai, Junichi; Hoshi, Hiroko; Masuda, Yukie; Yamai, Junko; Okamoto, Koji
PA Tanaka Precious Metal Ind, Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 05301884	A	19931116	JP 1992-129667	19920422
PRAI	JP 1992-129667		19920422		

OS MARPAT 120:337782
GI For diagram(s), see printed CA Issue.
AB Pt complexes [I; R = dibasic carboxylate anion], useful as anticancer agents (no data), are prepared in high purity from dihalo complexes II (X = halo) and purified by removing impurity ions with reverse osmosis. A mixture of K2PtCl6 and trans-1,2-cyclohexanediamine was dissolved in H2O to give 96% dichloro complex II (X = Cl), which in an aqueous suspension was stirred with an aqueous solution of AgNO3 in a dark room, AgCl was filtered, the filtrate was passed through a reverse osmosis membrane at 30 kgf/cm2 to remove various ions, the filtrate was concentrated, decolorized and treated with

oxalic acid to give 80% I (R = oxalate) containing Ag+ 0.3, NO3- 5, Cl- 2, and K+ <1 ppm, vs. 20.0, 20, 10, and 5 ppm, resp., without reverse osmosis.

L6 ANSWER 33 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:234810 CAPLUS
DN 120:234810
TI Optically pure cis-oxaloto(trans-1,2-cyclohexanediamine)Pt(II) and process for resolving optical isomers of a platinum complex compound
IN Tozawa, Takeshi; Komoda, Yasunobu; Ohnishi, Junji; Masuda, Yukie; Taniuchi, Junichi; Nakanishi, Chihiro; Okamoto, Koji; Ohnishini, Yuko
PA Tanaka Kikinzoku Kogyo K. K., Japan
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

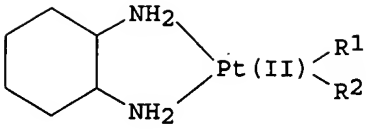
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 567438	A1	19931027	EP 1993-830160	19930409
	EP 567438	B1	19990113		
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
	JP 06287021	A	19941011	JP 1992-129668	19920422
	JP 06211883	A	19940802	JP 1993-19508	19930112
	US 5298642	A	19940329	US 1993-43577	19930407
	US 5338874	A	19940816	US 1993-43901	19930407
	ES 2125320	T3	19990301	ES 1993-830160	19930409
PRAI	JP 1992-129668	A	19920422		
	JP 1993-19508	A	19930112		

AB A process of optically resolving an optically active platinum complex consisting of a mixture of a D-isomer and an L-isomer uses HPLC with a column packed with a chiral filler. The chiral filler may be, for example, a cellulose ester derivative, a cellulose carbamate derivative, an amylose carbamate derivative, a polymethacrylic acid ester and β- and γ-cyclodextrin. An optically pure cis-oxalato (trans-1-1,2-cyclohexanediamine) Pt(II) separated from a D-isomer by this process is found to be remarkedly effective as a raw material for preparing a carcinostatic agent. Complete optical purity of the compound is reflected in a lower m.p. as compared with that of an impure substance.

L6 ANSWER 34 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1994:144135 CAPLUS
DN 120:144135
TI Preparation of cis-platinum complexes with 1,2-diaminocyclohexane as antitumor agents
IN Okamoto, Koji; Hoshi, Hiroko; Nakanishi, Chihiro
PA Tanaka Precious Metal Ind, Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 05194332	A	19930803	JP 1992-23219	19920113
	JP 07076230	B	19950816		
	US 5290961	A	19940301	US 1993-3306	19930112
	EP 617043	A1	19940928	EP 1993-830118	19930325
	EP 617043	B1	20011031		
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
PRAI	JP 1992-23219	A	19920113		

GI



I

AB The title complexes I (R1, R2, and Pt forms Q1-Q6) are provided; the configuration of the 1,2-diaminocyclohexane is cis-, trans-d-, trans-l. K chloroplatinate and trans-l-1,2-cyclohexanediamine were reacted to give dichloro(trans-l-1,2-cyclohexanediamine) Pt(II) complex (II). II was treated with AgOAc; AgCl was removed by filtration; the filtrate was concentrated, treated with KI and active C, and filtered; the filtrate was treated with oxalic acid to give cis-oxalate(trans-l-1,2-diaminocyclohexane) Pt(II) complex. The obtained product was highly pure.

L6 ANSWER 35 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1990:68684 CAPLUS
DN 112:68684
TI Platinum complexes and their use as antitumor agents
IN Nishi, Seiichi; Ohishi, Kazuo; Izawa, Kunisuke; Shiio, Tsuyoshi; Suami, Tetsuo
PA Ajinomoto Co., Inc., Japan
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 310260	A2	19890405	EP 1988-308469	19880914
	EP 310260	A3	19911211		
	R: DE, FR, GB, IT				
	JP 01156990	A	19890620	JP 1988-211695	19880826
	US 5041579	A	19910820	US 1988-257899	19880923
PRAI	JP 1987-241720	A	19870926		
	JP 1988-211695	A	19880826		

OS MARPAT 112:68684
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Pt complexes, useful as antitumor agents, of cis-diaminocyclohexanol or cis-diaminocyclohexane have the formulas I, IV [Z = COCO, COCHR9, SO2, Q, COCHR10Co; R1-R8 = H, hydroxy, provided that ≥1 of these is hydroxyl, and there is not more than 1 hydroxyl on each C atom constituting the cyclohexane ring; R9 = H, hydroxyl, C1-5 alkyl, Ph; R10 = H, hydroxyl, amino which may optionally be substituted, C1-5 alkyl, C1-5 alkoxy, Ph, or phenoxy; in the case of cyclohexane: use III or IV with R1-R8 = H] with the proviso that Pt complexes of 2-deoxystreptamine in which X2 is the residue of a dicarboxylic acid derivative are excluded. The following compds. were prepared (methods given): cis-oxalato-(1/2,3)-2,3-diamino-1-cyclohexanolplatinum(II), cis-sulfato-(1/2,3)-2,3-diamino-1-cyclohexanolplatinum(II), cis-glycolato-(1/2,3)-2,3-diamino-1-cyclohexanolplatinum(II), cis-oxalato-1,3-diaminocyclohexaneplatinum(II), cis-sulfato-1,3-diaminocyclohexaneplatinum(II), cis-cyclobutane-1,1-dicarboxylato-1,3-diamino-cyclohexaneplatinum(II), cis-sulfato-2-deoxystreptamineplatinum(II), (+)-cis-sulfato-(1/2,3)-2,3-diaminocyclohexanolplatinum(II), and (-)-cis-sulfato-(1/2,3)-2,3-diaminocyclohexanolplatinum(II). Various compds. of those made were

tested in female ICR/ICJ mice against sarcoma-180 cells, in female BDF1 mice against L 1210 cells, in female BDF mice against colon-38 cells, and against cisplatin-resistant L 1210 cells, showing effective results in each case.

L6 ANSWER 36 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1988:603718 CAPLUS
DN 109:203718
TI Synthesis and characterization of diastereomeric (substituted iminodiacetato)(1,2-diaminocyclohexane)platinum(II) complexes
AU Hoeschele, James D.; Farrell, N.; Turner, W. R.; Rithner, Christopher D.
CS Parke-Davis Pharm. Res. Div., Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SO Inorganic Chemistry (1988), 27(23), 4106-13
CODEN: INOCAJ; ISSN: 0020-1669
DT Journal
LA English
AB [Pt(DACH)L] [DACH = (R,S)- and (R,R)-1,2-diaminocyclohexane; H2L = RN(CH2CO2H)2, R = Me, CH2CH2OH, CH2Ph] were prepared, purified, and characterized by spectroscopic techniques (1H, 13C, and 195Pt NMR; fast-atom bombardment mass spectra; IR) and by the measurement of selected phys. properties (pH, pKa, conductivity, and mol. wts.). The data are consistent with the formation of 2 diastereomeric complexes in unequal proportions in which L2- appears to be bonded as a pseudofacial tridentate chelate. One arm of the ligand forms a stable 5-membered-ring O,N-chelate while the other arm appears to be involved in ion-pair formation (zwitterion-like) involving the carboxylate anion and the formally pos. Pt(II) central metal atom. An antitumor-active impurity was present in predictably inactive bulk complexes of the type PtN3O. The need to characterize unequivocally and certify the purity of prospective antitumor complexes is emphasized.

L6 ANSWER 37 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1978:608921 CAPLUS
DN 89:208921
TI Antitumor activity of 1,2-diaminocyclohexaneplatinum complexes against Sarcoma-180 ascites form
AU Kidani, Yoshinori; Inagaki, Kenji; Iigo, Masaaki; Hoshi, Akio; Kuretani, Kazuo
CS Fac. Pharm. Sci., Nagoya City Univ., Nagoya, Japan
SO Journal of Medicinal Chemistry (1978), 21(12), 1315-18
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
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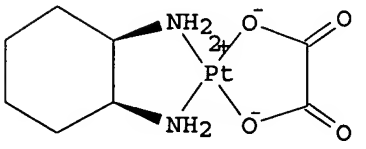

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AB The antitumor activity of the cis, trans-d, and trans-l title compds. was evaluated using Sarcoma-180 ascites in ddN mice. The antitumor activity varied with the conformation of their nonleaving groups. The highest therapeutic index was shown by oxalato(cis-1,2-diaminocyclohexane)platinum (I) [61913-68-6]. The cis complexes were more effective than the trans ones. LD values are given and structure-ability relationships are discussed.

L6 ANSWER 38 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1978:599862 CAPLUS
DN 89:199862
TI The cis platinum(II) complexes of 1,2-diaminocyclohexane isomers
IN Kitani, Yoshinori; Inagaki, Kenji
PA Japan
SO Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 53031648	A	19780325	JP 1976-106509	19760906
	JP 60041077	B	19850913		
	US 4169846	A	19791002	US 1978-924320	19780713
PRAI	JP 1976-106509	A	19760906		
	US 1977-775216	A1	19770307		

OS MARPAT 89:199862
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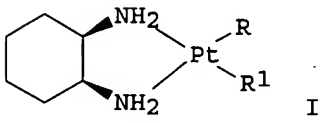

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AB I (R, R1 = halo; RR1 = O2CCO2, O2CH2CO2, O2CCHMeCO2) were prepared Thus, reaction of 5 g cis-diaminocyclohexane with 18 g aqueous K2(PtCl4) 12 h at room temperature gave 12 g I (R = R1 = Cl) (II). AgNO3 (6.8 g) was added to 3 g aqueous II, the mixture stirred 2-3 h in the dark, 4.8 g K oxalate added, the reaction mixture kept 8 h at room temperature 1.5 to give I (R = O2CCO2)(III). Anticarcinogenic data of I were shown against tumor L1210 and P388 and Sarcoma 180A in mice. LD50 of II and III were 11.3 and 37.5 mg/kg in mice (i.p.).

L6 ANSWER 39 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1978:436817 CAPLUS
DN 89:36817
TI Antitumor activity of platinum complexes of 1,2-diaminocyclohexane isomers
AU Speer, Robert J.; Hall, Larry M.; Stewart, David P.; Ridgway, Helen J.; Hill, Joseph M.; Kidani, Yoshinori; Inagaki, Kenji; Noji, Masahide; Tsukagoshi, Shigeru
CS Dep. Chem., Wadley Inst. Mol. Med., Dallas, TX, USA
SO Journal of Clinical Hematology and Oncology (1978), 8(2), 44-50
CODEN: JCHODP; ISSN: 0162-9360
DT Journal
LA English
AB Platinum complexes of 1,2-diaminocyclohexane were synthesized and tested as antileukemic agents against L1210 in mice. In most cases the (-)-trans-1,2-diaminocyclohexane complex was the most effective.

L6 ANSWER 40 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1978:16014 CAPLUS
DN 88:16014
TI Preparation and antitumor evaluation of water-soluble derivatives of dichloro(1,2-diaminocyclohexane)platinum(II)
AU Schwartz, Paul; Meischen, Sandra J.; Gale, Glen R.; Atkins, Loretta M.; Smith, Alayne B.; Walker, Ernest M., Jr.
CS VA Hosp., Charleston, SC, USA

SO Cancer Treatment Reports (1977), 61(8), 1519-25
CODEN: CTRRDO; ISSN: 0361-5960
DT Journal
LA English
AB The structure of the antitumor agent NSC-194814 [dichloro(1,2-diaminocyclohexane)platinum(II)] [52691-24-4] was modified by replacing the chlorides with organic or inorg. anions. Eighteen new Pt complexes were so isolated and their antitumor properties against the L1210 leukemia in C57BL/6 + DBA/2 mice were evaluated. Most of the complexes were readily soluble in water and some had enhanced antitumor activity compared to the parent dichloro complex. In addition, increased solubility with retention of
significant antitumor activity was obtained by oxidizing the parent dichloroplatinum(II) complex with halogen or peroxide to give 2 Pt(IV) complexes. Some previously reported Pt complexes with P, Se, or Te electron-donor ligands were also synthesized and assessed for antitumor action, but these did not show appreciable activity.

L6 ANSWER 41 OF 41 CAPLUS COPYRIGHT 2007 ACS on STN
AN 1977:400298 CAPLUS
DN 87:298
TI Synthesis and anti-tumor activities of platinum(II) complexes of 1,2-diaminocyclohexane isomers and their related derivatives
AU Kidani, Y.; Inagaki, K.; Saito, R.; Tsukagoshi, S.
CS Nagoya City Univ., Nagoya, Japan
SO Journal of Clinical Hematology and Oncology (1977), 7(1), 197-209
CODEN: JCHODP; ISSN: 0162-9360
DT Journal
LA English
AB Pt(II) complexes with cis- [1436-59-5], d-trans [21436-03-3], and l-trans-1,2-diaminocyclohexane [20439-47-8] were prepared and tested for antitumor activity. The Pt(II) complexes included the Cl, oxalate, malonate, and methylmalonate salts and the uracil complexes. The l-trans-1,2-diaminocyclohexane complexes showed the greatest neoplasm inhibiting activity. In contrast, complexes of Cu and Ni with 1,2-diaminocyclohexane were inactive. The conformational difference observed in this study may give very important information in the study of the mechanism of Pt complexes.

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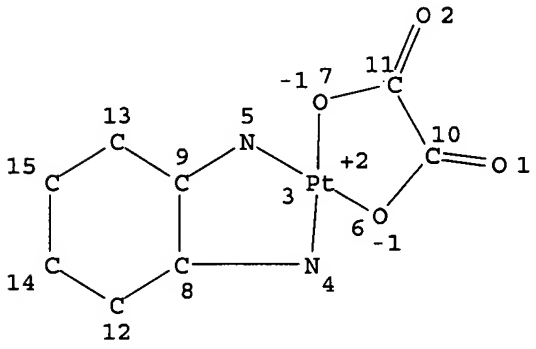

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